FEATURED ACTIVITIES of the DIVISION OF EXTRAMURAL RESEARCH AND TRAINING
October 2002

MEETINGS

The Role of Environmental Agents in Cardiovascular Disease
August 6-7, 2002
Durham Marriott at the Civic Center, Durham, NC

Cardiovascular disease represents the primary source of mortality in the industrialized world. The etiologies of cardiovascular diseases (CVDs) are multifactorial and include diet, genetics, and lifestyle. Findings over the last several years have made it clear, however, that environmental factors, such as ambient particulate matter, aldehydes, and polyaromatic hydrocarbons are also associated with pathophysiological changes in the cardiovascular system, cardiac malformations, and death due to CVD. However, relative to other organ systems, there has been little research into the effects of environmental agents on the cardiovascular system.

Recent advances in the fields of signal transduction, genetics, molecular biology, and epidemiology make expansion of research efforts in this area very timely. In addition, some environmental health science and cardiovascular researchers have successfully bridged the gap between these disciplines, resulting in innovative approaches to the study of environmentally induced CVD. Therefore, enhanced collaboration between these disciplines is seen as vital to the success of these efforts.

The format of the workshop, with emphasis on breakout sessions, was designed to enhance interactions among research scientists that will lead to identification of gaps in knowledge, appropriate questions for future research, innovative uses of existing technology and ideas for new technologies (including animal models), and types of collaborations needed to address these issues.

The workshop was cosponsored by NIEHS, EPA, NHLBI, and the American Heart Association Council on Epidemiology and Prevention and the AHA Expert Panel on Population and Prevention Science. Members of the organizing committee included Drs. Pat Mastin (NIEHS), Robert Devlin, Stacey Katz, and Gail Robarge (US EPA), Ken Ramos (Texas A&M University), Aruni Bhatnagar (University of Louisville), Wayne Cascio (UNC-Chapel Hill), John Godleski (Harvard School of Public Health), Murray Mittleman (Beth Israel Deaconess Medical Center), and Eser Tolunay (NHLBI).

Meeting Highlights
The workshop had more than 110 attendees. Most of the participants were environmental health scientists, but a good representation of cardiologists and cardiovascular researchers also attended. The major activities of the workshop were the six breakout sessions, which covered the following topics: Cardiovascular Epidemiology, Particulate Air Pollution and Myocardial Infarction, Environmental Agents and Vascular Disease, Environmental Modulation of Myocardial Excitability, Cardiovascular Oxidative Stress and Environmental Pollutants, and Environmental Toxicity and Cardiovascular Development. The workshop was very successful in bringing researchers from different fields together to discuss these issues. There was universal agreement that inclusion of multiple perspectives greatly enhanced the discussions. Research needs that were identified by the participants included more epidemiology and screening programs to identify agents, research to define the characteristics of toxicants and exposures, new animal models (or new application of existing models), identification of susceptibility factors (such as age and pre-existing diseases), and research to better understand the molecular targets in the cardiovascular system and to identify potential biomarkers. The workshop will hopefully act as a starting point for more activities, and collaborations, in this relatively understudied area.

The products of the meeting will include publication of the identified research needs and development of a document to serve as a framework for future program planning in this area.

Comparative Mouse Genomics Centers Consortium Symposium 2002
Human Gene Variation: From SNPs to Phenotypes
July 28-30, 2002
Seattle, Washington

The NIEHS Division of Extramural Research and Training initiated the Comparative Mouse Genomics Centers Consortium (CMGCC) Program in May 2001. The CMGCC scientific program falls under the auspices of the NIEHS Environmental Genome Project (EGP), a multidisciplinary, collaborative program that is focused on examining the relationships between environmental exposures, inter-individual sequence variation in human genes and disease risk in U.S. populations. The EGP, as it is organized today, has three phases. Phase 1 involves the systematic identification and genotyping of single nucleotide polymorphisms (SNPS) in cell cycle and DNA repair environmental response genes. Phase 2, of which CMGCC is a part, involves functional analysis of human DNA polymorphisms. Phase 3 will involve population-based epidemiology studies of human DNA polymorphisms. The CMGCC program is designed to develop transgenic and knockout mouse models based on

human DNA sequence variants in environmentally responsive genes. These mouse models will be used as tools to improve our understanding of the biological significance of the human DNA polymorphisms identified during Phase 1. This cooperative agreement program is comprised of an NIEHS Extramural team, including Drs. Velazquez and Packenham, Ms. Winters and Ms. McDuffie, and five University Centers with close to one hundred individuals.

CMGCC Centers:
MD Anderson Cancer Center, University of Texas, Dr. David Johnson – Center Director
Harvard Medical School, Dr. Raju Kucherlapati – Center Director
University of Washington, Dr. Warren Ladiges – Center Director
University of Cincinnati, Dr. Peter Stambrook – Center Director
University of Texas at San Antonio, Dr. Jan Vijg – Center Director

This Symposium was the first annual meeting of the CMGCC. The meeting was organized to introduce the CMG Centers to the Scientific Community and to promote strong Consortium interactions between the Centers principal investigators, post – doctoral fellows, staff and students. The symposium addressed how genetically engineered mouse models can be used to study environmentally induced human diseases

Meeting Highlights:
Over 100 individuals attended the meeting, including scientists from the U.S. and abroad. The meeting was two and one-half days. The topics for the first day of the meeting were DNA repair, cell cycle control, and gene function and regulation. Each Center director gave a general overview of his center followed by scientific presentations from Center Investigators. The evening session of the first day included a scientific poster session. The poster session consisted of projects from graduate students, post-docs and junior faculty. During each day of the symposium, notable scientists presented keynote addresses:

- "History of Mouse Genetics" - *Dr. Muriel Davisson*, Senior Staff Scientist, The Jackson Laboratory, Bar Harbor Maine

- "Natural Genetic Variation" - *Dr. Leland Hartwell*, Nobel Laureate, President and Director, Fred Hutchinson Cancer Research Center, Seattle, Washington

- "Our Changing Perception of the Terms "Mutation" and "Haplotype" - *Dr. Daniel W. Nebert*, Professor of Environmental Health and Pediatrics and Developmental Biology, University of Cincinnati Medical Center

During the second day of the meeting, distinguished speakers presented scientific lectures in the following areas:

SNP Variants
- "SNPing in the Human Genome" – *Debbie Nickerson*, University Of Washington
- "Patterns of Human DNA Sequence Variation" – *J. Claiborne Stephens*, Genaissance Pharmaceuticals
- "SNP Assessment in the Human Population" – *Leonid Kruglyak*, Fred Hutchinson Cancer Research Center

SNP Epidemiology
- "Folate, DNA Repair and Colorectal Neoplasia" **–** *Cornelia Ulrich*, Fred Hutchinson Cancer Research Center
- "Winnowing Seeds from the Chaff: Do any of the Large Number of Polymorphic Variants in DNA Repair Genes Impact Individual Cancer Risk" **–** *Harvey Mohrenweiser*, Lawrence Livermore National Laboratories

ENU Mutagenesis
- "Mouse ENU Mutagenesis" – *Monica Justice*, Baylor College of Medicine

Pheonomics
- "Image Based Phenotyping – The Visible Mouse" **–** *G. Allen Johnson*, Duke University Medical Center
- "Mouse Models of Diabetes and Atherosclerosis" **–** *Renee Le Boeuf*, University of Washington
- "Small Animal Imaging for Serial Characterization of Developing Mouse Embryos" – *Kenneth Krohn*, University of Washington

*****

Built Environment - Healthy Communities, Healthy Homes, Healthy People: Multilevel, Interdisciplinary Research Approaches
July 15-16, 2002
Research Triangle Park, NC

The built environment is defined as part of the overall ecosystem of our earth. It includes land-use planning and policies that impact our communities in urban, rural and suburban areas. It encompasses all buildings, spaces and products that are created, or modified, by people. It includes our homes, schools, workplaces, parks/recreation areas, business areas and roads. It extends overhead in the form of electric transmission lines, underground in the form of waste disposal sites and

subway trains, and across the country in the form of highways (adapted from Health Canada, 1997).

Dr. Srinivasan, Mr. O'Fallon and Dr. Tyson, CEMBB/DERT, organized this meeting, which was co-sponsored by the NIH Office of Behavioral and Social Science Research and the NIH Office of Rare Diseases. The purpose of the conference was to focus on the state of the science and explore future directions in conducting research on the built environment and health. It built upon the past workshops convened by NIEHS and the knowledge the agency has garnered from Health Disparities projects it has supported. The meeting was well attended, with over 100 participants. It was held in conjunction with the Health Disparities Grantee Meeting. A report based on the proceedings of this meeting will be available October 2002.

Meeting Highlights

The meeting was divided into three sessions. The first session titled "Environmental Health and Sustainable Communities" highlighted the importance of including environmental health in policy deliberations that in the long term create communities that are sustainable. The presentations focused on providing some broad based framework for the discussion on built environment and the creation of sustainable communities which incorporate improved environmental and public health. Sustainable communities are defined as those that seek to balance the social, economic, cultural, and the ecological infrastructure with human health and development. The second session entitled "Health Impacts" discussed the creation of communities that are environmentally healthful that requires an understanding of the impact of the structure of the built environment and urban ecosystems on air and water quality in homes, offices, and industry, the system of transportation and the emissions from automobiles, etc. This session highlighted the importance of planning that is cognizant of environmental health in the creation of healthy communities, healthy homes and healthy people. The final session titled "Partnerships for Environmentally Healthful Communities" focused on the creation of communities that are cognizant of the environment and the health of its citizens that require partnerships among policy makers, governments, researchers, communities, and health specialists who have an interdisciplinary perspective. This session highlighted several programs that have developed partnerships to create sustainable communities and that have a positive impact on public health.

Each session involved three grantees from the Health Disparities program responding to the speakers in relation to their project funded by NIEHS.

Meeting Recommendations

- The need for more effective measures of built environment, such as indicators for sustainable communities.
- Health impacts of better planning and use of more efficient or alternative energy (in areas such as, transportation, agriculture, land use, architecture, community design, etc).
- Need to incorporate cost effectiveness of adopting environmentally sustainable technologies.
- Need to develop an interdisciplinary program approach for training, within agencies and in research.
- Improve communication strategies which promoting community participation.
- Develop multi-levels of measurement and analyses that incorporate longitudinal models (including SES, biology, neighborhoods, physical environment etc).
- Identify factors that mediate and moderate built environment health effects.
- Methods and channels to translate research findings to policy.

*****

Arsenic in New England: A Multidisciplinary Scientific Conference
http://www.dartmouth.edu/~cehs/ArsenicConference/IndexAS.html
May 29-31, 2002
Manchester, New Hampshire

The Superfund Basic Research Program (SBRP) has an established history in supporting multi-disciplinary conferences and workshops developed by SBRP grantees that focus on research topics important to the mission of the Program. SBRP sponsored scientific conferences are considered an integral component of the program's mission to disseminate scientific information. Conferences are just one of several approaches used by the Program for dissemination of research findings not only to the scientific community but to the many different audiences/stakeholders that may use information generated by the Program for decision-making.

The Dartmouth Program with its research emphasis on arsenic has been very proactive in developing the New Hampshire Arsenic Consortium. Arsenic exposure is of particular concern in New England, where soils and waters in many regions naturally contain levels of arsenic that are substantially higher than those found in other areas of the United States. The New Hampshire Arsenic Consortium brings together university scientists and the New Hampshire Departments of Environmental Services and Health and Human Services and the US Geological Survey. Formation of this group had led to increased communication among the agencies and has resulted in the design and undertaking of inter-agency projects to collect data to support risk assessments. One of the outcomes of this collaboration was the "Arsenic in New England" conference, which the NIEHS SBRP supported.

Exposure to arsenic in drinking water represents a significant health problem for people around the world. Arsenic tops the list

of U.S. Environmental Protection Agency's list of hazardous chemicals at toxic waste sites. Though exposure to arsenic has been linked to increased risk of cancer, heart disease, diabetes and reproductive disorders in humans, most studies have involved people exposed to elevated levels in the workplace or in parts of the world where drinking water contamination is exceptionally high. Scientists have little direct information about the effects of arsenic at levels found commonly in the United States. In addition, the way arsenic interacts with other substances in biological systems--such as the cells in human bodies -- is poorly understood.

This two-and-a-half day, multidisciplinary scientific conference provided participants with an overview of new findings regarding arsenic in New England by researchers in disciplines ranging from geology to molecular biology. Scientific presentations and discussions focused on arsenic's natural occurrence; patterns of anthropogenic use and disposal in New England; mechanisms of action as a toxin; effects on human health; environmental impact and movement through ecosystems; and regulation and remediation strategies. One goal of this cross-disciplinary forum was to provide an opportunity for synthesis - a more comprehensive view of arsenic and its impact on human health.

Meeting Highlights
The conference had more than 170 attendees representing a diverse community including academicians, State Health and Environmental Department officials from New Hampshire, Massachusetts, Maine, Vermont, and Wisconsin, Federal agency representatives from EPA and USGS, environmental consultants and private industry representatives. The two-and-a-half meeting consisted of five scientific platform sessions and an evening poster session. The platform sessions covered the following topics: Arsenic Occurrence and Geochemistry, Local Arsenic Issues – Controls and Mechanisms, Biology and Epidemiology of Arsenic, Epidemiology of Environmental Arsenic Exposure and Remediation and Regulation of Arsenic.

The first session on occurrence and geochemistry summarized the prevalence of arsenic in ground water in the New England states and the likely sources for the arsenic. In general, the predominate source of arsenic in groundwater and stream sediments is rock-based arsenic and the levels seen appear to be strongly correlated with water chemistry, geologic provinces and rock chemistry while there is a weak correlation with past agriculture land-use. Moreover, well by well measurements for arsenic is still the most reliable method to quantitate arsenic levels. Studies presented demonstrated that even with significant geochemical and geospatial data, the microenvironment has significant influence over arsenic levels making model predictions very unreliable as currently developed.

The second session on controls and mechanisms provided more in depth discussions on the influence of water and rock chemistry and geologic formations on the fate and transport of arsenic through the aquifer.

The third and fourth sessions focused on biology and epidemiology. These sessions provided the audience with the latest scientific advances concerning the potential impact of arsenic on human health. Presentations focused on molecular and cellular mechanisms for cardiovascular effects, expression of DNA repair genes and arsenic as an endocrine disruptor; its role in cancer, vascular disease and diabetes. Epidemiology studies discussed arsenic exposure and reproductive effects and cancer risks. In addition, there was a public health discussion on arsenic exposure through indirect water pathways such as bathing and issues that communities face when told there is arsenic in the water.

The last session of the conference focused on primary prevention; what remedial steps can be taken to reduce arsenic levels in drinking water and the regulatory policies that govern drinking water standards for arsenic. The meeting ended with a panel discussion that grounded all of the participants in the reality of the arsenic problem. Discussion by state health officials reminded us that the public would like answers to their questions "What does this arsenic concentration in my drinking water mean to the health of me and my family?" and "What can we do about it?" There are still no easy answers to these questions.

*****

Bioremediation and Biodegradation: Current Advances in Reducing Toxicity, Exposure and Environmental Consequences
July 9-12, 2002
Pacific Grove, California

The United States has thousands of hazardous waste sites, most of which are legacies of many decades of industrial development, mining, manufacturing and military activities. Biodegradative processes and bioremediation solutions form a large part of the current science and technology directed at treatment of environmental contaminants at these hazardous waste sites. As there has been an explosion of cutting-edge basic research in these areas over the past several years and, as the SBRP has a long history of supporting research in area of bioremediation, it was timely for the Program to bring together leaders in the field to discuss innovations in the field of monitoring and remediating as well as specific advances in the degradation of PCE's, PAHs, MTBE and nitrophenol. Reoccurring themes of discussion centered on the implications of improved analytical technologies and the bioavailability of contaminants in the context of biodegradative processes.

The conference was sponsored by the Superfund Basic Research Program and organized and chaired by SBRP grantees Jerome Kukor, (University of Michigan program) and Lily Young (New York University). Dr. William Suk presented the

keynote address, “The Superfund Basic Research Program: A Model for Meeting the Interdisciplinary Research Needs of the Nation.” Scientists and students from across the country met to address current issues at the interface areas of toxicity reduction, exposure assessment, and evaluation of environmental consequences. The conference included a mixture of formal (platform lectures) and less-formal (roundtable discussions and poster sessions) sessions, allowing all participants opportunities to express their views. Sessions included:

I. Approaches to Overcome Bioavailability Limitations in Bioremediation;
II. New Discoveries in Microbial Degradation of Persistent Environmental Contaminants;
III. Biological Activity and Potential Toxicity of the Products of Biodegradation;
IV. New Methods to Monitor and Assess the Effectiveness of Remediation Processes; and
V. Strategies for Remediation of Mixed Contaminants.

Conference proceedings will be available on CD, and it is anticipated that the platform lectures will be published in *Environmental Health Perspectives.*

*****

DERT PAPERS OF NOTE

Martyn T. Smith
University of California Berkeley
P30ES01896

Gene Polymorphisms and Altered Risk of Adult Acute Lymphocytic Leukemia

Background: Although the clinical and pathological aspects of leukemia are well known, little is understood about the genes that influence susceptibility to this complex disease. Certain gene polymorphisms have been shown to alter the risk of development of leukemia and these variations can interact with diet, other environmental exposures, and individual immune function to be major determinants of susceptibility. This researcher has previously reported polymorphisms in a folate metabolizing gene with a decreased risk of acute adult lymphocytic leukemia (ALL). The research hypothesis is that the protective effect is due to an increase in the flux of folate compounds available for DNA synthesis and subsequent reductions of uracil in the DNA. Accumulation of uracil in DNA and its subsequent removal during excision repair processes can result in DNA double strand breaks which are necessary for chromosomal translocations and deletions.

Advance: Polymorphisms in methionine synthase (*MS*), cytosolic serine hydroxymethyltransferase (*SHMT*), and a double or triple 28-base pair tandem repeat in the promoter region of thymidylate synthase (*TS*) were studied and all were found to reduce ALL risk dramatically. When individuals had both the SHMT polymorphisms and the triple repeats in *TS* or the *MS* and *SHMT* polymorphisms the ALL risk was even further reduced.

Implications: This research illustrates an association between changes in folate metabolic pathways which affect *TS* and lymphocytic leukemia risk that may underscore the importance of compromised DNA fidelity and insufficient folate intake in the development of ALL. DNA integrity is dependent on the bioavailability of deoxynucleotides, particularly in cells with high replication rates such as those found in the hematopoetic system and epithelium. Moreover, low intake of folic acid and other factors such as vitamins B2, B6, and B12 may increase ALL risk in persons with high risk genotypes. A combination of unfavorable genotypes, diet, and vitamin B intake and balance may conceivably be the key factor in susceptibility to ALL. Continued research may lead to dietary and nutritional modifications to decrease the risk of genetically susceptible individuals.

Citation: Skibola CF, Smith MT, Hubbard A, Shane B, Roberts AC, Law GR, Rollinson S, Roman E, Cartwright RA, and Morgan GJ. Polymorphisms in the thymidylate synthase and hydroxymethyltransferase genes and risk of adult acute lymphocytic leukemia. *Blood* 2002; 99, 10:3786-3791.

*****

Patricia A. Buffler and Martyn T. Smith
University of California, Berkeley
R01ES09137 and P42ES04705

Discovery of Gene Translocations in Childhood Acute Myeloid Leukemia

Background: The cause and progression of childhood leukemia is of great interest to patients and their families and physicians as well as basic and epidemiologic researchers. Understanding how the disease starts and proceeds has implications on how it can be prevented and/or treated. Recent studies have shown that the genetic changes necessary to allow the development of the disease occur *in utero*. Leukemia may not develop for several years suggesting additional molecular events that are necessary for disease development. Childhood acute myeloid leukemia (AML) comprises about 20% of all childhood leukemia and represents a group of diseases with a variety of molecular subtypes. After a peak incidence of leukemias in infants with translocation of the *MLL* gene, children with AML exhibit the same range of abnormalities as adults, the most frequent of which is a fusion of the *AML1* and *ETO* genes.

Advance: Unlike the age associated peak in leukemia incidence seen with the *MLL* translocation, the *AML1-ETO* fusion increases slowly during childhood and is constant throughout life. Similar leukemias sometimes develop after chemotherapy for other cancers adding additional evidence that further triggers are necessary for leukemia development. These researchers analyzed genomic sequences for 5 AML patients. Two of the patients were older than 10 years at the time of diagnosis indicative of a protracted postnatal latency period. Further studies showed that the genomic fusion sequences persist during remission.
Implications: These studies indicate that the genetic alterations leading to AML in children occur *in utero*, possibly as an initiating event that requires secondary genetic alterations to cause leukemia. This raises the question of whether translocation positive-preleukemic stem cells formed *in utero* may persist into adulthood providing a lifetime supply of cells that may progress to AML given the correct secondary genetic alteration.

Citation: Wiemels JL, Xiao A, Buffler PA, Maia AT, Ma X, Dicks BM, Smith MT, Zhang L, Feusner J, Wiencke J, Pritchard-Jones K, Kempski H, and Greaves M. In utero origin of t(8;21) *AML1-ETO* translocations in childhood acute myeloid leukemia. *Blood*, 15 May 2002; 99, 10:3801-3805.

*****

Bruce J. Aronow
University of Cincinnati College of Medicine
R01ES08822

Microarray Techniques Used to Identify Genes Controlling the Development of the Mouse Gastrointestinal Tract

Background: Understanding the molecular basis of gene expression along the anterior-posterior (A-P) axis of the mammalian gastrointestinal (GI) tract is a critical need for determining the genes that are involved in the embryonic development of the GI tract, how gene expression occurs, and how development progresses. This understanding has been lacking, but using novel microarray gene expression techniques can lead to rapid discovery of candidate genes responsible for GI development along the length of the GI tract.

Advance: This team of investigators hypothesized that patterns of gene expression along the A-P axis could be defined at the gene and molecular level by analyzing expression profiles of large numbers of genes. Microarrays containing over 8,600 complementary DNA (cDNA) sequences were used to define expression profiles for mouse stomach, duodenum, jejunum, ileum, cecum, proximal colon, and distal colon. Highly expressed cDNAs were classified based on segmental expression patterns and protein function. The investigators found 571 cDNAs which were expressed at least 2-fold higher than reference in at least one GI region. Most of the genes displayed sharp boundaries at anatomically defined locations. Boundaries were especially sharp for genes encoding proteins that function in intermediary metabolism, transport, and cell-cell communication–functions critical for the proper coordination of GI function. Genes with distinct expression profiles were compared with mouse and human genomic sequence for promoter analysis and gene discovery.

Implications: The anatomically defined regions of the GI tract can also be defined by the pattern of expression profiles from genes located in and controlling functions in these regions. Distinctions in gene expression patterns between the small and large intestines were much less striking than those between the stomach and the small and large intestines. The investigators also identified new genes not previously known to be expressed in GI tissue. Identification of genes co-regulated along the A-P axis provides a basis for new insights, research, and gene discovery relevant to GI development, differentiation, function, disease, and therapeutic interventions.

Citation: Bates MD, Erwin CR, Sanford LP, Wiginton D, Bezerra JA, Schatzman LC, Jegga AG, Ley-Ebert C, Williams SS, Steinbrecher KA, Warner BW, Cohen MB, and Aronow BJ. Novel genes and functional relationships in the adult mouse gastrointestinal tract identified by microarray analysis. *Gastroenterology* 2002;122:1467-1482.

*****

Harold F. Hemond

Massachusetts Institute of Technology
P42ES04675

Water Nitrate Effects Arsenic Valence and Concentration in an Urban Lake

Background: Anyone who has ever read a mystery novel knows that arsenic is acutely toxic and that its harmful effects have been known and exploited for hundreds if not thousands of years. However, at doses found in some drinking water supplies and private wells in parts of the United States and other parts of the world such as Chile, Taiwan, and Bangladesh, arsenic can have chronic, long-term effects such as causing skin, bladder, and prostate cancer. In the environment, inorganic arsenic is found in oxidized and reduced states. The oxidized form is known as arsenate and this valence state is much more carcinogenic than the reduced form known as arsenite.

When lakes and streams become anoxic, underlying sediments tend to release arsenic and iron compounds. In most cases, the arsenic originates from industrial pollution. Arsenate can be bound up by iron particles rendering the arsenic unavailable to wildlife and humans who may drink or otherwise come into contact with the water. Therefore, any agent that changes this intricate balance or the valence state of the arsenic compounds may have important public health consequences.

Advance: This publication describes how nitrate contamination alters the balance of arsenic and iron complexes. Nitrates accumulate in water systems through agricultural and lawn fertilizer use and from animal waste runoff. Nitrate is a powerful oxidant and thus has the potential to oxidize arsenite released from lake and stream sediments to the more toxic arsenate. Depending on the concentration of iron in the water, arsenate may accumulate in the water.

Implication: With the new drinking water standard for arsenic of 10 µG/l, some municipalities will have to pay high costs to bring their water supplies into compliance to protect the health of the people they serve. Understanding the causes of arsenic contamination and other factors influencing the concentration of arsenic and its oxidation-reduction cycle may influence the method used to reduce the arsenic concentration. Methods to prevent the introduction of nitrates into drinking water supplies may be important in keeping the arsenic in the lake and stream sediments and out of the water supply.

Citation: Senn DB, Hemond HF. Nitrate controls on iron and arsenic in an urban lake. *Science* 2002, vol. 296:2373-2376.

*****

Richard D. Kolodner
University of California at San Diego
R01ES11040

New Discoveries in the Development of Colon Cancer

Background: Several forms of human colorectal cancer exist with the most frequent being the sporadic form. A variety of genetic mutations have been implicated in the development of this deadly disease. Sporadic defects in DNA mismatch repair genes play a role in either the initiation or progression of a number of tumor types. This observation suggests that other DNA repair genes could be involved in the development of colon cancer. One such gene known as *Flap endonuclease 1* (*Fen1*) was investigated in this study. *Fen1* is required for DNA replication and repair, and defects in the gene encoding Fen1 are known to cause accumulation of mutations and genomic rearrangements. Using gene knockout techniques, the investigators introduced a mutation into *Fen1*.

Advance: Genetic analysis of the mice used in this study showed that none were homozygous for the *Fen1* mutation. This suggests that absence of *Fen1* expression leads to embryonic lethality. Most of the mice heterozygous for the *Fen1* mutation appeared normal, but further studies showed that when combined with a mutation in the adenomatous polyposis coli gene, double heterozygous animals have increased numbers of adenocarcinomas and decreased survival.

Implication: This study suggests that insufficiency of *Fen1* expression may not make a difference to a cell undergoing normal replication, but if the cell cycle is perturbed by mutations in oncogenes or tumor suppressor genes, additional levels of a least some gene products might be necessary to accommodate the change in rates of cell division. If one or more products necessary for replication and repair is not present in the right quantities, the result may be detrimental to genomic stability. These results imply that a quantitative measure of the expression of some of these gene products may be useful as prognostic indicators of disease.

Citation: Kucherlapati M, Yang K, Kuraguchi M, Zhao J, Lia M, Heyer J, Kane MF, Fan K, Russell R, Brown AMC, Kneitz B, Edelmann W, Kolodner RD, Lipkin M, and Kucherlapati R. Haploinsufficiency of Flap endonuclease (Fen1) leads to rapid tumor progression. *PNAS*, July 23, 2002; 99; 15:9924-9929.

*****

Scott Ballinger
University of Texas Medical Branch
R03ES09318

Mitochondrial Damage Leads to Atherosclerosis

Background: Reactive species (RS) are made up of a group of reactive oxygen and nitrogen species that can alter the biological functions of essential molecules such as lipids, proteins, and DNA. Numerous studies have linked RS with the development of atherosclerotic disease which remains the leading cause of death in the Western world. Although the exact sequence of events in this process is yet to be determined, RS likely play an important role in vascular cell dysfunction and atherosclerosis probably through oxidative damage to the mitochondrial genome. In this study, the investigators examined the contribution of mitochondrial oxidant generation and DNA damage to the progression of atherosclerotic lesions in human arterial specimens and a mouse model prone to atherosclerosis.

Advance: Mitochondrial DNA damage correlated with the extent of atherosclerosis in the human tissue and in the susceptible mice. The DNA alterations were seen prior to the development of atherogenesis in the mice suggesting a causative relationship. In addition, mice deficient in manganese superoxide dismutase, a mitochondrial antioxidant enzyme, exhibited early increases in mitochondrial DNA damage and a phenotype of accelerated atherogenesis.

Implications: These studies suggest that mitochondrial DNA damage may result from RS production in vascular tissues and may also be an early event in the development of atherosclerosis. Additional research confirming these results may lead to earlier detection of individuals at risk for atherosclerotic disease and improved methods to prevent of reverse the formation of atherosclerotic plaques through the use of antioxidant therapies.

Citation: Ballinger SW, Paterson C, Knight-Lozano CA, Burow DL, Conklin CA, Hu A, Reuf J, Horaist C, Lebovitz R, Hunter GC, McIntyre K, and Runge MS. Mitochondrial Integrity and Function in Atherogenesis. *Circulation* 2002; 106:544-549.

*****

David A. Schwartz
Duke University Medical Center
R01ES07498, P01ES09607, and U19ES11375

Receptor Variant that Confers Decreased Immune Function is a Marker for Resistance to Atherosclerosis

Background: The ability to mount a prominent inflammatory response to a bacterial challenge confers an advantage in innate immune defense; however, the effects of intravascular inflammation lead to proatherogenic effects. The focus of this study was to determine if genetic variants in the toll-like receptor 4 (TLR4) that confer differences in the inflammatory response due to bacterial lipopolysaccharide are related to the development of atherosclerosis. The hypothesis tested was that efficient immune defense offers an early advantage but at a cost of chronic vascular damage in later years.

Advance: An epidemiologic study was carried out in 810 persons in which the team screened for TLR4 polymorphisms. The extent and progression of atherosclerosis was also assessed. Fifty-five individuals were found to have the Asp299Gly TLR4 polymorphism. These individuals had lower levels of certain proinflammatory cytokines and other inflammatory agents. While these subjects were more susceptible to severe bacterial infections, they had an almost 50% reduction in the risk of carotid arterial atherosclerosis.

Implications: The polymorphism identified in this study attenuates receptor signaling and diminishes the inflammatory response to gram negative bacteria along with decreasing the risk of atherosclerosis. This study provides further evidence that an efficient innate immune defense against bacteria is associated with long-term intravascular inflammatory stress leading to the development of atherosclerosis.

Citation: Kiechl S, Lorenz E, Reindl M, Wiedermann CJ, Oberhollenzer F, Bonara E, Williet J, Schwartz DA. Toll-like receptor 4 polymorphisms and atherogenesis. *New England Journal of Medicine* 2002, 347; 3:185-192.

*****

Joseph Kiesecker
Pennsylvania State University

R01ES11067

Frog Limb Deformities: Synergism Between Pesticide Exposure and Parasite Infection

Background: For the past ten years, biologists have been puzzled by the apparent epidemic of frog limb deformities seen in Canada and the United States especially in the West, Midwest, and Northeast. Researchers are unsure whether the dramatic increase relates to increased awareness or environmental changes, but a variety of studies have sought to link the deformities and the dwindling number of frogs to ultraviolet radiation exposure, chemical pollution, predation, parasites, or disease outbreaks. Earlier reports by Kiesecker have suggested that extremely dry climatic conditions cause increased exposure to ultraviolet radiation which in turn causes immune dysfunction leading to decreases in population density resulting from increased susceptibility to diseases and parasite infection.

Advance: In the current study, Kiesecker reports field and laboratory studies that conclusively demonstrate that trematode infection was required for the development of limb deformities in wood frogs. Deformities were more common at sites adjacent to agricultural runoff. The laboratory studies corroborate the association between pesticide exposure and increased infection with pesticide-mediated immunocompetency as the apparent mechanism.

Implication: The immune effects in the laboratory studies were seen at pesticide levels within the current EPA drinking water standards. Similar adverse effects are seen in other amphibians in other regions and may be explained by the widespread use of pesticides. Whether similar adverse effects are seen in other animal species remains to be determined, but the fact that these effects are seen at relatively low pesticide concentrations, suggests major public health implications and the possibility of the need for more stringent pesticide regulation.

Citation: Kiesecker JM. Synergism between trematode infection and pesticide exposure: A link to amphibian limb deformities in nature? *PNAS*, July 23, 2002, v. 99:15, 9900-9904.

*****

E. William Spannhake
The Johns Hopkins Bloomberg School of Public Health
P30ES03819

Adding Environmental Insult to Injury: Oxidant Pollutants Add to Inflammatory Cytokine Release in Response to Rhinoviral Infection

Background: Cold viruses and environmental pollutants cause respiratory cells to release inflammatory cytokines which contribute to the general malaise people feel when they have respiratory symptoms. Cytokines are cellular inflammatory components that cause inflammation, which leads to the release of fluids, swelling, and other symptoms. Not everyone reacts the same way to the combined insult of respiratory infection and pollutant exposure. Asthmatics are particularly susceptible to the combined adverse effects.

Advance: Researchers at The Johns Hopkins Bloomberg School of Public Health determined that the combined effects of NO_2 or O_3 and rhinoviral infection in cultured respiratory cells rapidly increased the release of the inflammatory cytokine interleukin-8 through oxidant-dependent mechanisms. The combined effects ranged from 42% to 250% greater than additive for NO_2 and from 41% to 67% for O_3. The effect was lessened by treatment of the cells with the antioxidant *N*-acetylcysteine.

Implication: These results indicate that oxidant pollutants can increase the production of proinflammatory cytokines by rhinoviral infected cells and suggest that viral-induced inflammation in upper and lower airways may be exacerbated by concurrent exposure to ambient levels of oxidants commonly encountered in the indoor and outdoor environments.

Citation: Spannhake EW, Reddy SPM, Jacob DB, Yu X-Y, Saatian B, Tian J. Synergism between rhinovirus infection and oxidant pollutant exposure enhances airway epithelial cell cytokine production. *Environmental Health Perspectives*, 110:7, 665-670.

*****

Robert E. Gawley - University of Miami
Daniel G. Baden - University of North Carolina at Wilmington
T32ES07320 and P30ES005705

Does *Pfiesteria* Produce Toxins? New Research Suggests Not

Background: The bacteria *Pfiesteria piscicida* has received a lot of attention since it was first reported to be responsible for

fish kills and human illnesses along the Atlantic coast in 1992. The dinoflagellate was reported to produce one or more toxins in certain strains and at certain periods in a proposed intricate life cycle which is said to contain "amoeba-like" stages. Other researchers in this field have been unable to reproduce these results and thus a major controversy has grown. Defenders of the original hypothesis say that these researchers are using the wrong strain of bacteria. The detractors say that the toxins are produced by another microbe that has contaminated the *Pfiesteria* cultures and thus, *Pfiesteria* is not the culprit.

Advance: A team led by researchers at the University of Miami has found that a close relative to *P. piscicida, Pfiesteria shumwayae*, does not produce the ichthyotoxins postulated to kill fish and harm humans. Simple removal of the bacteria from contaminated water by centrifugation resulted in water that was non-toxic to healthy fish. When the bacteria itself is applied to the fish, sores similar to those reported as evidence of toxin exposure are seen. The researchers speculate that similar infections may make fish more susceptible to other microbes such as a highly pathogenic fungus.

Implication: While not definitively proving that *Pfiesteria* species are or are not responsible for large fish kills along the east coast, this work suggests that the original hypothesis of the bacteria producing ichthyotoxins responsible for the kills may not be the actual pathogenic mechanism. Additional research soon to be published documenting the chemical structure and potency of a *Pfiesteria* toxin will provide additional information surrounding this controversy.

Citation: Berry JP, Reece KS, Rein KS, Baden DG, Haas LW, Ribeiro WL, Shields JD, Snyder RV, Vogelbein WK, Gawley RE. Are *Pfiesteria* species toxicogenic? Evidence against production of ichthyotoxins by *Pfiesteria shumwayae*. *PNAS*, U.S.A. Early Addition. 2002 Aug 5.

*****

Tracy M. Reed and Charles V. Vorhees
Children's Hospital Medical Center, Cincinnati, Ohio
T32ES07051

Enzyme Deficient Mice Display Hyperactivity and Impaired Learning Ability

Background: The family of calcium/calmodulin dependent phosphodiesterases (CaM-PDE) act as a potential point of interaction between the Ca^{2+} and cyclic nucleotide signaling pathways. The three known CaM-PDE genes *PDE1A-C*, are expressed in the central nervous system. *PDE1A* is expressed throughout the brain with high levels in the cerebellum and lower levels in the striatum. *PDE1B* is expressed predominantly in regions of the brain with high dopaminergic innervation such as the striatum and cerebellum. *PDE1C* is also expressed predominantly in the striatum. The expression of these genes in the striatum and other evidence that cyclic nucleotides and calcium are principal second messengers of the signal transduction pathways in the striatum suggest that CaM-PDEs may play a role in motor control. To investigate this hypothesis, these investigators generated knock-out mice lacking the *PDE1B* gene.

Advance: These mice showed increased hyperactivity, as compared to normal mice, after acute exposure to D-methamphetamine. Since the mice lacked the enzyme, hydrolysis of the cyclic nucleotides could not occur and was confirmed with analysis of tissue slices. The knock out mice and mice with one copy of the functioning gene demonstrated spatial-learning deficits in experiments employing a Morris maze.

Implication: These results indicate that enhancement of cyclic nucleotide signaling by inactivation of *PDE1B*-mediated cyclic nucleotide hydrolysis plays a major role in dopaminergic function. The results of these experiments support the conclusion that regulation of intracellular cyclic nucleotide concentration is important in the cellular processes that underlie learning and memory.

Citation: Reed TM, Repaske DR, Snyder GL, Greengard P, Vorhees, CV. Phosphodiesterase 1B knock-out mice exhibit exaggerated locomotor hyperactivity and DARPP-32 phosphorylation in response to dopamine agonists and displayed impaired spatial learning. Journal of *Neuroscience*, June 15, 2002; 22(12):5188-5197.

*****

David C. Christiani
Harvard School of Public Health
P01ES06409 and P30ES00002

Glutathione S-Transferase and p53 polymorphism Are Associated with Increased Lung Cancer Risk

Background: Genetic susceptibility is one of the primary hypotheses used to explain why a minority of smokers develop lung cancer. Polymorphisms of genes involved in metabolism of carcinogens have been studied as possible attenuators of risks for lung cancer. The family of glutathione S-transferase (GST) enzymes are important components of carcinogen metabolism so polymorphic differences in these enzymes may be responsible for at least part of the differences in risk. GST π is the most

expressed metabolic enzyme in the lung and it is encoded by a polymorphic gene *GSTP1*. These polymorphisms are a consequence of a single base-pair substitution which leads to a single amino acid change in the enzyme. This substitution results in lower enzymatic activity and is associated with higher DNA adduct formation in human lymphocytes. A polymorphism in another GST gene, *GSTM1-null*, results in the total loss of enzymatic function.

Polymorphic genes involved in cell cycle regulation, apoptosis, and tumor suppression have also been studied as possible risk factors for lung cancer. *p53* is one of these genes and is one of the most commonly mutated genes in all human cancers. Several studies have shown that the polymorphic *p53* gene is associated with a higher risk of lung cancer.

Individually, functional polymorphisms of these genes have been studied as risk factors for lung cancer; however, small sample sizes have prevented the investigation of possible increases in risk associated with having two or more at risk polymorphisms. Christiani and colleagues have carried out such an investigation of "double variants" in a large Caucasian population. Because these double variants may promote lung cancer at an earlier age, a subgroup of people 55 and younger was examined separately.

Advance: In the whole population, those with double variants had a higher risk of lung cancer compared with controls. The *GSTP1* and *GSTM1-null* double variants had a relative risk only slightly higher (60%) than controls; however the *GSTP1* and *p53* double variant were twice as likely to develop lung cancer. In the younger group, the relative risks were 4- and 5-fold higher respectively.

Implication: Specific double variants of *GSTP1*, *GSTM1-null*, and *p53* double variants are associated with higher lung cancer risks. This susceptibility is highest among younger individuals. Additional studies will help elucidate the possible mechanisms involved in the steps leading to carcinogenesis. Although the combined double variant risks generally had a greater than additive effect, larger sample sizes are needed to consider differences in gender and to clarify the association with early onset lung cancer.

Citation: Miller DP, Liu G, De Vivo I, Lynch TJ, Wain JC, Su L, Christiani DC. Combinations of the variant genotypes of *GSTP1, GSTM1*, and *p53* are associated with an increased lung cancer risk. *Cancer Res*. 2002 May 15;62(10):2819-23.

*****

GRANTEE HONORS and AWARDS

NIEHS-supported investigator, Dr. Brendan H. L. Lee, M.D., Ph.D., of Baylor College of Medicine, has been awarded a prestigious Howard Hughes Investigator Award. The announcement was made on May 28. Dr. Lee is one of 12 of the nation's top physician-scientists to be appointed as Howard Hughes Medical Institute investigators in an innovative program to improve the translation of basic science discoveries into enhanced treatments for patients.

Dr. Peter Stacpoole, Professor of Medicine, Biochemistry and Molecular Biology at the University of Florida, was inducted as a Fellow of the Royal College of Physicians of London, on July 25, 2002, in London, England.

STAFF HONORS and AWARDS

Dr. Allen Dearry, OPD/CEMBB, and Mr. Joseph Hughes, OD/WETP, were recipients of the Secretary's Award for Distinguished Service, which was presented at the DHHS awards ceremony Wednesday, June 12. A group award was bestowed on the pair "For dedicated support to the health and safety of emergency responders, remediation workers and the community at the World Trade Center disaster." The ceremony was held in the Great Hall, Hubert H. Humphrey Building, Washington, DC.

The NIEHS Toxicogenomic Research Consortium Group received the 2002 NIH Director's Award at a ceremony held Wednesday, June 19, at NIH. The award was "For Outstanding Efforts Conceptualizing, Initiating, and Implementing the NIEHS Toxicogenomics Research Consortium." Awardees included *Dr. Anne Sassaman , OD; Dr. William Suk, OPD; Drs. Michael McClure and Jerrold Heindel, OPD/OSTB; Dr. Bennett Van Houten, OPD/PAB; Drs. Jose Velazquez and Claudia Thompson, OPD/CEMBB; Dr. Linda Bass and Ms. RoseAnne McGee and Ms. Michelle Mayo, OPO/SRB; Ms. Jackie Russell, OPO/GMB; Ms. JoAnn Lewis, OPO/RCB*, Drs. Raymond Tennant, Richard Paules, Pierre Bushell, and Cynthia Afshari, and Mr. Stan Stasiewicz from DIR, and Dr. Samuel Wilson, Deputy Director.

Ms. Martha Barnes, OPD/PAB, is a member of a trans-NIH committee, operating under the Office of Research on Women's Health, that received an NIH Merit Award "For exceptional accomplishments in revising NIH policies and procedures for monitoring inclusion and facilitating gender analysis in biomedical research," at the Office of the Director Honor Awards Ceremony 2002 held August 14, at NIH.

STAFF ACTIVITIES

Mr. O'Fallon, OPD/CEMBB, collaborated with Drs. T. Nastoff and D. Drew from the Agency for Toxic Substances and Disease Registry (ATSDR) and Dr. J. Phillips from the National Institute for Nursing Research to organize and convene a roundtable meeting on nursing and environmental health on August 26-27. The three agencies jointly sponsored the meeting which focused on the following themes: Research, Education and Translation to Practice. The interagency planning committee invited experts from around the country to participate in the roundtable meeting with the anticipated outcome of identifying gaps in these three areas and recommending next steps to address the identified needs. A final meeting report will be available in November.

Dr. Srinivasan, OPD/CEMBB, chaired a plenary track thematic session at the American Sociological Association national meeting in Chicago, Illinois, on August 18 entitled "Profiling in Health," which examined the affects of social environment in prevention of disease and access to care and the growing health disparities among low income minority populations.

Mr. Hughes, OD/WETP, and staff hosted the NIEHS/Worker Education and Training Program Training Skilled Support Personnel meeting in Research Triangle Park, North Carolina on August 15. The focus of the meeting was on to discuss future safety and health training program initiatives regarding weapons of mass destruction incident response with a particular focus on what training is appropriate for skilled support personnel. The meeting also focused on the feasibility of establishing a national registry of trained personnel to respond to future terrorist actions. Staff attending the meeting and participating in various activities included *Ms. Beard, Mr. Outwater, Ms. Thompson, and Ms. Chaney, OD/WETP.*

Dr. Collman, OPD/CEMBB, organized and chaired two sessions on Children's Environmental Health at the International Society of Environmental Epidemiology and International Society of Exposure Analysis joint meeting in Vancouver, BC, Canada on August 12. The topics for the sessions were exposures assessment in large scale epidemiologic studies of children's environmental health and using biomarkers to translate exposure to health effects. Representatives from all of the Centers of Children's Environmental Health and Disease Prevention Program gave presentations on new findings from their research.

Dr. Shreffler, OPD/OSTB, participated in a panel discussion on Postdoctoral Fellowships at the Workshop on Grant Writing for Success sponsored by the University of North Carolina Postdoc Association in Chapel Hill, NC, on July 31. The Workshop was designed to assist individuals in postdoctoral positions in uncovering funding opportunities, understanding types of granting mechanisms, and getting started in the grant-writing process.

Ms. Anderson, OPD, served as the moderator for the session "Biological Activity and Potential Toxicity of the Products of Biodegradation" at the Bioremediation and Biodegradation: Current Advances in Reducing Toxicity, Exposure and Environmental Consequences meeting, which was held July 9-12, in Pacific Grove, California.

Dr. Van Houten, OPD/PAB, and *Dr. Weis, OPD/OSTB*, participated in a Working Group on Ethical, Legal, Social and Policy Issues in Toxicogenomics held at the Woodrow Wilson International Center for Scholars Washington, D.C., July 18-19. Dr. Van Houten gave a lecture entitled, Establishing Toxicogenomics: Necessary Steps and New Initiatives.

Mr. Hughes, OD/WETP, attended the International Association of Fire Fighters Instructor Development Conference in Las Vegas, Nevada on July 17-19. He presented on the Weapons of Mass Destruction Report to the National Response Team Subcommittee.

Dr. Srinivasan, Mr. O'Fallon and Dr. Tyson, OPD/CEMBB, organized a meeting entitled "Built Environment - Healthy Communities, Healthy Homes, Healthy People: Multilevel, Interdisciplinary Research Approaches," which was held on July 15-16, in Research Triangle Park, North Carolina in conjunction with the Health Disparities grantee meeting. The meeting was co-sponsored by the Office of Behavioral and Social Science Research. The Office of Rare Diseases provided additional funding. The purpose of this conference was to focus on the state of the science and explore future directions in conducting research on built environment and health.

Dr. Mastin, OPD/OSTB, was appointed to the Steering Committee of the National Asthma Education and Prevention Program, and was invited to make a brief presentation on NIEHS-funded asthma research at the annual meeting of the Steering Committee, June 10, in Arlington, Virginia.

Dr. Heindel, OSTB/OPD, gave a presentation, "Endocrine Disruptors: A View from NIEHS " at the Endocrine Disruptors Gordon Conference at Mt. Holyoke College, Massachusetts, July 9.

Dr. McClure, OPD/OSTB, has been appointed to a three-year term on the Hitchings and Elion Award Advisory Committee of the Triangle Community Foundation. Drs. Hitchings and Elion shared the 1998 Nobel Prize in Physiology or Medicine for a series of scientific breakthroughs in pharmaceutical chemistry that revolutionized the world of drug design. Founded with Nobel Prize funds, the Triangle Community Foundation, in partnership with the Burroughs Wellcome Fund, supports awards to outstanding young investigators in the Triangle region of Wake, Durham, Orange and Chatham Counties. The George H.

Hitchings New Investigator Award in Biomedical Research and the Gertrude B. Elion Mentored Medical Student Award is an annual national competition that honors with remembrance the strong belief of the two Nobel Laureates in the high value of supporting the training and mentoring of the next generation of young scientists.

Dr. McClure, OPD/OSTB, accepted an invitation to serve on the faculty of the American Association for the Advancement of Science sponsored 2002 Science Laboratory Management Course for Young Investigators funded by the Howard Hughes Medical Institute and Burroughs Wellcome Fund. The course was attended by 245 M.D., M.D./Ph.D., or Ph.D. young scholars. His presentation, entitled: "Science Fair to Science Fare: A Darwinian Budgetary View of the Scientist Species" presented an overview of the changing budget needs of and strategies for fueling and refueling an independent research laboratory from start-up onward. His presentation was invited to be published in *Science* in an upcoming 2002 issue. The HHMI plans to publish the course as a multimedia manual.

Dr. McClure, OPD/OSTB, represented the NIH at the Appalachian College Association's Federal Agency and Foundation Briefing for Research Program Faculty Development held June 10-11, in Asheville, North Carolina. Dr. McClure presented an overview of the Extramural Research Grant Programs and Opportunities entitled: "The National Institutes of Health: Encouraging the Biomedical Research that improves Public Health." Attendees of the meeting were college presidents, senior administrators, and research faculty from 33 private sector colleges from Kentucky, Tennessee, North Carolina, Virginia and West Virginia. He also participated in small group and individual conferences on NIH funding mechanisms and opportunities.

Dr. McClure, OPD/OSTB, presented the Legacy Lecture "Population and the Environment" at the opening session of the Frontiers in Reproduction (FIR) Research Training Course at the Marine Biological Laboratory (MBL), Woods Hole Massachusetts on May 19th. The course is a research concepts, strategies and technology applications "wet" lab career development experience mentored (1:2) and instructed by an international faculty of nearly 40 world-class scientists. Sixteen outstanding young scholars, selected by an annual international, peer-reviewed competition, were awarded scholarships to attend the FIR course.

Ms. Beard, OD/WETP, attended and presented at the Brownfields Interagency Taskforce Meeting in Washington, DC on May 30.

Mr. Hughes and Mr. Outwater, OD/WETP, presented at the 12th Annual Construction Safety and Health Conference and Exposition on May 21-23 in Chicago, Illinois. The Worker Education and Training Program along with Center to Protect Workers' Rights, NIOSH, the Construction Safety Council and many other organizations sponsored this conference. The conference shared information and ideas about effective safety and health interventions and how to move "best practices" from inception to practical implementation.

UPCOMING MEETINGS and WORKSHOPS

NIEHS and ATSDR are jointly sponsoring a meeting, "Thyroid Hormone & Brain Function: Translating Molecular Mechanisms to Population Risk," September 23-25. The purpose of this conference is to bring together a multidisciplinary group of research scientists (epidemiologists, clinicians, basic and molecular biologists, developmental biologists and toxicologists, and endocrinologists) in a joint forum to discuss the current state of emerging, multidisciplinary knowledge relevant to the role of thyroid hormones in brain development and the effects of exposures to environmental agents on this system. Focus will be on maternal thyroid status and neurological function of the offspring; basic studies on brain development; the role of thyroid hormones in brain development; the effects of environmental agents on thyroid hormone action during brain development; and future directions for research with emphasis on the use of genomics, genetically modified animals, imaging and translation of basic and toxicological research into public health benefit. The information gained on the state of the science and data gaps will be used to direct future collaborations between the two agencies.

The annual Center Directors' meeting will be held October 21-22, in Seattle, Washington. It will be hosted by the Environmental Health Sciences Center at the University of Washington.

NIEHS (through the Worker Education and Training Program), National Institute for Occupational Safety and Health (NIOSH), Johns Hopkins Education and Research Center for Occupational Safety and Health, and MidAtlantic Public Health Training Center are co-sponsoring the Technical Workshop on the Worker Training in a New Era: Responding to New Threats. This conference will draw upon lessons learned from recent terrorist attacks to help attendees better understand and anticipate the safety and health-training needs of workers who would be required to respond to terrorist incidents in the future. The conference will be held in Baltimore, Maryland on October 26-27. On October 25, the semi-annual WETP Awardee Meeting will be held.

Tthe Brownfields 2002 Conference will be held in Charlotte, North Carolina on November 13-15. This national conference will showcase brownfields cleanup, redevelopment and policy issues. Included will be a meeting of the awardees of the Brownfields Minority Worker Training Program to discuss progress in this new training program and promote the model of community based environmental job training program. Representative from local, state, and federal Brownfields programs will

also be invited. The meeting will provide an excellent setting to promote the WETP Minority Worker Training Program and Brownfields Minority Worker Training Program.

The University of Arizona will host the 2002 annual national meeting of the Superfund Basic Research Program (SBRP), November 3-6 in Tucson, Arizona. The intent of this year's meeting, "Transitioning Basic Science into Practical Applications to Meet Environmental and Public Health Challenges," is to highlight technology transfer activities that have evolved from basic laboratory research to practical applications, with discussion on the pathways that investigators have taken to achieve this. An important aspect of this goal is to present "emerging technologies" that have the potential to enhance the capacity of basic research to address Superfund hazardous waste issues. In addition to the scientific sessions, running concurrently will be an administrators' meeting, designed to enhance the sharing of ideas among the administrators, and an outreach workshop, highlighting the major themes of the outreach cores. Detailed information about the meeting can be found on http://benson.niehs.nih.gov/sbrp/annualconf.html.

STAFF CHANGES

Recruitments:
Dr. Janice Allen joins *OPO/SRB* as a Scientific Review Administrator. After working as a research technician and chemist at the University of North Carolina at Chapel Hill and the National Institutes of Health in Bethesda, respectively, studying the cell-cell and molecular interactions of pro- and anti-inflammatory mediators in arthritis, AIDS, and hepatic granulomas, Dr. Allen received her Ph.D. from North Carolina State University College of Veterinary Medicine in Cell Biology and Biotechnology where she subsequently joined the faculty and investigated the role of transforming growth factor beta and nitric oxide in endotoxin-induced uveitis.

Dr. Mike Humble joined *OPD/OSTB* on August 12 as a Health Sciences Analyst. Dr. Humble will work with the Toxicogenomics Research Consortium and the Collaborative Centers for Parkinson's Research Consortium. He is a native of Minnesota, and received his BA from St Olaf College and his MS from the Univ of Minnesota, both in Chemistry. The MS research and training focused on studies of nicotinic acetylcholine receptor protein binding sites for its ligand. Dr. Humble was a high school department chairman and chemistry teacher prior to earning his PhD in Toxicology from UNC-CH. His dissertation and post-doctoral research were performed in the laboratory of Dr. Ray Tennant, NIEHS, where he conducted research using transgenic mice to explore promoter regulation of transcriptional control of the carcinogenic process leading to a unique, unexpected form of skin tumor .

Dr. Brenda K. Weis joined *OPD/OSTB* as a Health Scientist Administrator in May 2002. She serves as the Extramural Toxicogenomics Research Coordinator and the Program Administrator for Metabonomics. Prior to joining OSTB, Dr. Weis served as a Scientific Review Administrator for SRB. She came to NIEHS from Agency for Toxic Substances and Disease Registry (ATSDR) in Atlanta, where she served as the Acting Deputy of the Office of the Associate Administrator for Science. During her 10-year employment at the ATSDR, Dr. Weis served as project leader for numerous multidisciplinary health investigations and was instrumental in developing science policy and setting environmental health research priorities for ATSDR and the Centers for Disease Control.

Mr. Larry Reed, has joined *OPD* as a Guest Researcher where he will be working on the Superfund Basic Research Program. He comes from EPA, where he has worked for the past 28 years, most recently as the Deputy Director (and Acting Director) of the Office of Emergency and Remedial Response. Among his positions, Mr. Reed has served previously as the Director of the Hazardous Sites Evaluation Division, Chief of the Compliance Information Branch (Office of Water Enforcement and Permits), Deputy Director of the Chicago Regional Planning and Management Division, and Chief of the Toxics Integration Branch (Office of Pesticides and Toxic Substances). He has an MPA from Harvard University.

Mr. Benigno Encarnacion has joined *OPO/GMB* as a Grants Financial Analyst.
Ms. Elizabeth McNair has joined *OPD/OSTB* as a secretary.
Ms. Anne Thompson has joined *OPD/PAB* as a secretary.
Mr. David Sedgley has joined *OPO/RCB* as a procurement technician.

Departures:
Dr. Jose Velazquez, OPD/CEMBB, is leaving DERT on September 20 to become Chief, Genomics and Proteomics Branch, in the Division of Basic Sciences at the National Institute of Alcohol Abuse and Alcoholism.